PRVD2008-13

Proposed Re-evaluation Decision

Benzisothiazolin-3-one

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Overview

What Is the Proposed Re-evaluation Decision?

After a re-evaluation of the antimicrobial benzisothiazolin-3-one, Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing continued registration for the sale and use of products containing benzisothiazolin-3-one in Canada.

An evaluation of available scientific information found that products containing benzisothiazolin-3-one do not present unacceptable risks to human health or the environment when used according to label directions. As a condition of the continued registration of benzisothiazolin-3-one uses, new risk-reduction measures must be included on the labels of all products. No additional data are being requested at this time.

This proposal affects all end-use products containing benzisothiazolin-3-one registered in Canada. Once the final re-evaluation decision is made, the registrants will be instructed on how to address any new requirements.

This Proposed Re-evaluation Decision is a consultation document[1] that summarizes the science evaluation for benzisothiazolin-3-one and presents the reasons for the proposed re-evaluation decision. It also proposes additional risk-reduction measures to further protect human health and the environment.

The information is presented in two parts. The Overview describes the regulatory process and key points of the evaluation, while the Science Evaluation provides detailed technical information on the assessment of benzisothiazolin-3-one.

The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document. Please forward all comments to Publications (please see contact information on the cover page of this document).

What Does Health Canada Consider When Making a Re-evaluation Decision?

The PMRA's pesticide re-evaluation program considers potential risks, as well as value, of pesticide products to ensure they meet modern standards established to protect human health and the environment. Regulatory Directive DIR2001-03, *PMRA Re-evaluation Program*, presents the details of the re-evaluation activities and program structure.

Benzisothiazolin-3-one, one of the active ingredients in the current re-evaluation cycle, has been re-evaluated under Re-evaluation Program 1. This program relies as much as possible on foreign reviews, typically United States Environmental Protection Agency (USEPA) Reregistration

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1 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

Eligibility Decision (RED) documents. For products to be re-evaluated under Program 1, the foreign review must meet the following conditions:

- it covers the main science areas, such as human health and the environment, that are necessary for Canadian re-evaluation decisions;
- it addresses the active ingredient and the main formulation types registered in Canada; and
- it is relevant to registered Canadian uses.

Given the outcome of foreign reviews and a review of the chemistry of Canadian products, the PMRA will propose a re-evaluation decision and appropriate risk-reduction measures for Canadian uses of an active ingredient. In this decision, the PMRA takes into account the Canadian use pattern and issues (e.g. the federal Toxic Substances Management Policy [TSMP]).

Based on the health and environmental risk assessments published in the 2005 RED, the USEPA concluded that benzisothiazolin-3-one was eligible for reregistration provided risk-reduction measures were adopted. The PMRA compared the American and Canadian use patterns and found the USEPA assessments described in this RED were an adequate basis for the proposed Canadian re-evaluation decision.

For more details on the information presented in this overview, please refer to the Science Evaluation section of this consultation document.

What Is Benzisothiazolin-3-one?

Benzisothiazolin-3-one is an antimicrobial used as a preservative in metalworking fluids, latex emulsions, aqueous-based paints and aqueous mineral slurries in industrial settings. It is also used as a formulant in a variety of other pesticide products as a material preservative.

Health Considerations

Can Approved Uses of Benzisothiazolin-3-one Affect Human Health?

Benzisothiazolin-3-one is unlikely to affect your health when used according to revised label directions.

Exposure to benzisothiazolin-3-one may occur when it is added to the material being treated (e.g. paint or metalworking fluids) or while using the treated material (e.g. painting, machinist handling metalworking fluids). Exposure may also occur when it is used as a formulant in other end-use products, through food or residential use, e.g. pet products. The PMRA considers two key factors when assessing health risks: the levels at which no health effects occur and the levels to which people may be exposed. The dose

levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers). Only uses for which exposure is well below levels that cause no effects in animal testing are considered acceptable for continued registration.

The USEPA concluded that benzisothiazolin-3-one was unlikely to affect human health provided that risk-reduction measures were implemented. These conclusions apply to the Canadian situation, and equivalent risk-reduction measures are required.

Environmental Considerations

What Happens When Benzisothiazolin-3-one Is Introduced Into the Environment?

Benzisothiazolin-3-one is unlikely to affect non-target organisms when used according to label directions.

The USEPA concluded that indoor uses of benzisothiazolin-3-one were not likely to result in unacceptable ecological risk to non-target organisms based on minimal exposure potential and did not conduct any quantitative ecological risk assessments. Similarly, the use of benzisothiazolin-3-one as a formulant occurs at no more than 0.1% of the formulation and is readily biodegraded in soil, greatly reducing the exposure potential for terrestrial and aquatic organisms. Runoff into surface water from the use of benzisothiazolin-3-one as a formulant was also expected to be low. The USEPA concluded that the reregistration of benzisothiazolin-3-one was acceptable and no mitigation measures were required. These conclusions apply to the Canadian situation, and no risk-reduction measures are required.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law. As a result of the re-evaluation of benzisothiazolin-3-one, the PMRA is proposing further risk-reduction measures for product labels.

Human Health

- Additional protective equipment to protect handlers.

Next Steps

Before making a final re-evaluation decision on benzisothiazolin-3-one, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will then publish a Re-evaluation Decision[2] document that will include the decision, the reasons for it, a summary of comments received on the proposed decision and the PMRA's response to these comments.

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2 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

Science Evaluation

1.0 Introduction

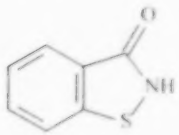
Benzisothiazolin-3-one is an antimicrobial used as a preservative in metalworking fluids, latex emulsions, aqueous-based paints and aqueous mineral slurries. It is also used as a formulant in a variety of other pesticide products.

Following the re-evaluation announcement for benzisothiazolin-3-one, the registrant of the technical grade active ingredient in Canada indicated its intention to provide continued support for all uses included on the labels of commercial end-use products in Canada.

The Pest Management Regulatory Agency (PMRA) used recent assessments of benzisothiazolin-3-one from the United States Environmental Protection Agency (USEPA). The USEPA Reregistration Eligibility Decision (RED) document for benzisothiazolin-3-one, dated 2005, as well as other information on the regulatory status of benzisothiazolin-3-one in the United States can be found on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

2.0 The Technical Grade Active Ingredient, Its Properties and Uses

2.1 Identity of the Technical Grade Active Ingredient

Common name	Benzisothiazolin-3-one
Function	Antimicrobial
Chemical family	Isothiazolone
Chemical name	
1. **International Union of Pure and Applied Chemistry (IUPAC)**	1,2-Benzisothiazol-3(2H)-one
2. **Chemical Abstracts Service (CAS)**	Benzisothiazolin-3-one
CAS Registry Number	2634-33-5
Molecular formula	C_7H_5NOS
Structural formula	
Molecular weight	151.2 amu

Registration Number	23197	28122	25712
Purity of the technical grade active ingredient	72% nominal (limits: 69.84–74.16)	72% nominal (limits: 69.85–74.10)	75% nominal (limits: 67–83)

Batch data for two of the three registered technical products were analyzed for 2,3,7,8-containing chlorinated dibenzo-p-dioxin isomers. Targeted 2,3,7,8 chlorinated dioxins were not detected at the detection limit of 0.01 ppb. Low levels of 1,2,3,4,6,7,8-HpCDD and OCDD as well as some non-targeted HxCDDs and HpCDD were present. Low levels of some 2,3,7,8-containing chlorinated dibenzofuran isomers were also present in one of the technical products.

Microcontaminant data were not submitted for the Thor GMBH product (Registration Number 28122).

2.2 Physical and Chemical Properties of the Technical Grade Active Ingredient

Property	Result
Vapour pressure at 25°C	3.7×10^{-4} Pa
Solubility in water at 20°C	1.1 g/L
n-Octanol–water partition coefficient	Log K_{ow} = 0.4
Dissociation constant	p*K*a = 7.18

2.3 Comparison of Use Patterns in Canada and the United States

Benzisothiazolin-3-one is an antimicrobial registered in Canada to be added as a preservative to metalworking fluids, latex emulsions, casein/rosin emulsions, emulsion paints, aqueous-based paints/coatings and aqueous mineral slurries in industrial settings. The maximum application rate as percent benzisothiazolin-3-one by weight of material treated is 0.048% for metalworking fluids, 0.016% for latex emulsions and 0.05% for aqueous-based paints and coatings and aqueous mineral slurries. The end-use products are formulated as solutions.

The American and Canadian use patterns were compared. Canadian uses are encompassed by American uses and the guarantees (9 to 20%) are the same in Canada and the United States. The maximum application rate as percent benzisothiazolin-3-one by weight of material treated in the United States is the same or higher than in Canada. All uses registered in Canada are also registered in the United States and the American use pattern is more extensive. Based on this comparison of use patterns, it was concluded that the USEPA RED for benzisothiazolin-3-one is an adequate basis for the re-evaluation of uses of benzisothiazolin-3-one as an active ingredient in pest control products in Canada.

All current uses in Canada are being supported by the registrants and were therefore considered in the re-evaluation of benzisothiazolin-3-one. Appendix I lists all benzisothiazolin-3-one products that are registered as of 1 January 2008, under the authority of the *Pest Control Products Act*.

Benzisothiazolin-3-one is also used as a formulant in other pesticide products in both Canada and the United States. These other pesticide products may be registered for use on food commodities, pet-related products, turf, or in other residential settings. In its risk assessment, the USEPA took into account the use of benzisothiazolin-3-one as a formulant at a maximum concentration of 0.1%. In Canada, benzisothiazolin-3-one is also typically present at 0.1% or less as a formulant in other pesticide products. Although the formulant uses of benzisothiazolin-3-one are also discussed here, a re-evaluation decision regarding the formulant uses will not be made at this time. Formulant issues are being addressed through PMRA formulant initiatives and Regulatory Directive DIR2006-02, *Formulants Policy and Implementation Guidance Document,* published on 31 May 2006.

3.0 Impact on Human Health and the Environment

In its 2005 RED, the USEPA concluded that the end-use products formulated with benzisothiazolin-3-one met the safety standard under the American *Food Quality Protection Act* and would not pose unreasonable risks or adverse effects to humans and the environment if used according to amended product labels.

3.1 Human Health

Toxicology studies in laboratory animals describe potential health effects resulting from various levels of exposure to a chemical and identify dose levels at which no effects are observed. Unless there is evidence to the contrary, it is assumed that effects observed in animals are relevant to humans and that humans are more sensitive to effects of a chemical than the most sensitive animal species.

Exposure to benzisothiazolin-3-one may occur through consumption of food or through residential or occupational uses. When assessing health risks, the PMRA considers two key factors: the levels at which no health effects occur and the levels to which people may be exposed. The dose levels used to assess risks are established to protect the most sensitive human population (e.g. children and nursing mothers).

3.1.1 Occupational Exposure and Risk Assessment

Occupational risk is estimated by comparing potential exposures with the most relevant endpoint from toxicology studies being used to calculate a margin of exposure (MOE). This is compared to a target MOE incorporating safety factors protective of the most sensitive subpopulation. If the calculated MOE is less than the target MOE, it does not necessarily mean that exposure will result in adverse effects, but mitigation measures to reduce risk would be required.

The USEPA's toxicological endpoints for assessing risk from occupational exposure are summarized in Appendix II.

Workers can be exposed to benzisothiazolin-3-one when it is added to the material being treated (e.g. paint or metalworking fluids), or while using the treated material (e.g. painting, machinist handling metalworking fluids).

3.1.1.1 Mixer/Loader/Applicator Exposure and Risk

Workers handling the formulated product

Five short- and intermediate-term dermal and inhalation exposure scenarios for handlers of formulated products were identified by the USEPA, representing the high end of industrial uses of the formulated product. Among the scenarios assessed in the RED, the following two exposure scenarios were considered relevant to the Canadian situation:

- Mixing/loading biocides containing benzisothiazolin-3-one using liquid open pour methods for the preservation of industrial process intermediate materials (e.g. adding an in-can preservative to paints, adhesives, slurries, oil/gas drilling fluids)

- Mixing/loading biocides containing benzisothiazolin-3-one using liquid open pour methods for preservation of metalworking fluids (i.e. exposure occurs either via loading and filling bulk tanks or machine sumps or setup/maintenance of the automatic metering systems)

Handler exposure analyses were performed using Chemical Manufacturers Association data. The liquid pour for preservatives scenario and the liquid pour for metalworking fluids scenario were based on an application rate of 0.050% and 0.032% benzisothiazolin-3-one by weight of material treated, respectively. Combined short- and intermediate-term dermal and inhalation risk was based on an oral no observed adverse effect level (NOAEL) of 5 mg/kg bw/day from a subchronic toxicity study in dogs and a dermal absorption factor of 41% based on a dermal study in rats.

The USEPA reported acceptable short- and intermediate-term combined dermal and inhalation MOEs of 1200 for the liquid pour for preservatives scenario and 5100 for the liquid pour for metalworking fluids occupational exposure scenario (i.e. greater than target MOE of 100) based on workers wearing a long-sleeved shirt, long pants and gloves. Although the 0.032% by weight of material treated for the metalworking fluid scenario represents the minimum amount of active ingredient handled per day, the maximum amount handled per day (i.e. 0.048% by weight of material treated) would still result in acceptable MOEs much greater than the target MOE of 100.

Workers handling products containing benzisothiazolin-3-one as a preservative

Four short- and intermediate-term dermal and inhalation exposure scenarios for handlers of products containing benzisothiazolin-3-one (e.g. paint or cleaning products) were assessed in the RED. The following two exposure scenarios were considered relevant to the Canadian situation:

- Applying paint containing benzisothiazolin-3-one using a brush or roller
- Applying paint containing benzisothiazolin-3-one using an airless sprayer

These scenarios were considered to represent high-end exposure scenarios and it was assumed that applying paint would be equal to or greater than exposure from applying building materials such as water-based adhesives, caulks, sealants, grouts, spackling, ready-mixed cements and ready-mixed wallboard compounds. Handler exposure analyses were performed using the Pesticide Handlers Exposure Database, Version 1.1, and the assumption that workers were wearing a long-sleeved shirt, long pants and no gloves. Combined short- and intermediate-term dermal and inhalation risk was based on an oral NOAEL of 5 mg/kg bw/day from a subchronic toxicity study in dogs, a dermal absorption factor of 41% based on a dermal study in rats, and the assumption that commercial painters apply five gallons of paint when using a brush or roller and 50 gallons when using an airless sprayer with an application rate of 0.050% benzisothiazolin-3-one by weight of material treated.

The USEPA reported an acceptable short- and intermediate-term combined dermal and inhalation MOE of 190 for the brush/roller scenario. The short- and intermediate-term combined dermal and inhalation MOE of 85 for the airless sprayer scenario was found to be below the target MOE of 100 (where the dermal MOE = 90 and the inhalation MOE = 1700). However, the USEPA determined that this scenario was not of concern because the paint matrix has the potential to reduce dermal absorption. Therefore, it was believed that a dermal MOE of 90 was likely an overestimate of risk and no further mitigation measures were required.

Machinists handling metalworking fluids

Handler long-term dermal exposure analyses were performed using computer modelling to estimate dermal exposure of machinists handling metalworking fluids. A dermal absorption factor of 41%, based on a dermal study in rats, was assumed. In the screening level assessment of handler long-term inhalation exposure, the model developed by the Chemical Engineering Branch of the USEPA Office of Prevention, Pesticides and Toxic Substances was used to estimate inhalation exposure of machinists handling metalworking fluids. It was assumed that airborne oil mist concentrations for metalworking operations were 5 mg/m^3 based on Occupational Safety and Health Administration's permissible exposure limit. Both long-term dermal and inhalation risks were based on an oral NOAEL of 5 mg/kg bw/day from a subchronic toxicity study in dogs, an exposure duration of eight hours and an application rate of 0.048% benzisothiazolin-3-one by weight of material treated.

The USEPA reported an acceptable long-term dermal MOE of 200 and an acceptable long-term inhalation MOE of 31,000 (target MOE = 100).

Conclusion

The percent active ingredient by weight of material treated used for each scenario in the RED risk assessments represents the maximum on Canadian labels (i.e. 0.048% for metalworking fluids and 0.05% for paints, latex emulsions and mineral slurries). The RED adequately addressed potential exposure scenarios associated with the Canadian uses of products containing benzisothiazolin-3-one, and conclusions derived from the RED apply to the Canadian situation.

Current Canadian end-use product labels for benzisothiazolin-3-one caution that the product is corrosive and causes severe eye and skin damage. The PMRA therefore requires that benzisothiazolin-3-one end-use product labels be amended to include the wearing of a long-sleeved shirt, long pants and chemical-resistant gloves, in addition to any personal protective equipment (e.g. goggles, faceshield) already on the labels. The proposed label amendments are listed in Appendix III.

3.1.1.2 Postapplication Exposure and Risk

Postapplication exposure may occur in industrial settings via inhalation and dermal exposure while maintaining industrial equipment. However, the USEPA did not assess occupational postapplication risks to industrial workers because dermal postapplication exposure to benzisothiazolin-3-one was considered to be minimal when compared to handler exposure. In addition, inhalation exposure was expected to be minimal because aerosol generation was not expected and the vapour pressure of benzisothiazolin-3-one is low.

3.1.2 Non-Occupational Exposure and Risk Assessment

3.1.2.1 Residential Exposure

Residential exposure is estimated using the MOE approach described in Section 3.1.1. The toxicological endpoints selected by the USEPA for assessment of risk from residential exposure are summarized in Appendix II.

In the United States, benzisothiazolin-3-one is registered for preservative use in paint and cleaning products. Risk to adults from applying paint and wiping or mopping hard non-porous surfaces using cleaning products containing benzisothiazolin-3-one was assessed. Only the risk to adult homeowners applying paint is relevant to the Canadian situation and is presented here.

Handler exposure analyses for paint application were performed using the Pesticide Handlers Exposure Database, Version 1.1, and the assumption that handlers would be wearing shorts and a short-sleeved shirt. Short-term dermal and inhalation risk was based on an oral NOAEL of 5 mg/kg bw/day from a subchronic toxicity study in dogs, a dermal absorption factor of 41% from a dermal study in rats, and the assumption that a homeowner applies two gallons of paint when using a brush or roller and 15 gallons when using an airless sprayer with an application

rate of 0.050% benzisothiazolin-3-one by weight of material treated. Acceptable adult handler combined (short-term dermal and inhalation) MOEs of 370 and 140 (target MOE = 100) were reported when applying paint using a brush or roller and when applying paint using an airless sprayer, respectively.

Postapplication exposure and risk from the use of benzisothiazolin-3-one as a formulant was also assessed using flea and tick pet spray products as a representative scenario. Dermal and inhalation applicator exposure (i.e. applying the aerosol pet flea and tick product), and toddler short-term dermal exposure (i.e. hugging exposed pet) and toddler short-term incidental oral exposure (hand-to-mouth activity) were assessed.

Handler exposure analyses were performed based on spraying a flea and tick pet spray product containing 0.1% benzisothiazolin-3-one. An adult handler combined (dermal and inhalation) MOE of 19,000 was reported (target MOE = 100), and a toddler incidental oral MOE was estimated to be 2500 (target MOE = 300). However, the toddler dermal MOE was estimated to be 33 (target MOE = 100) and was of concern. The USEPA determined that a percent formulation of 0.033% benzisothiazolin-3-one would result in an acceptable dermal target MOE of 100. Based on this, the USEPA required that all pet products containing benzisothiazolin-3-one as a formulant must contain a maximum of 0.033% benzisothiazolin-3-one in order to be eligible for reregistration.

The RED adequately addressed potential exposure scenarios associated with the Canadian residential uses of benzisothiazolin-3-one (i.e. homeowner applying paint, flea and tick pet spray product; postapplication exposure of toddlers to pet spray product). Thus, the conclusions derived from the RED are considered applicable to the Canadian situation. The flea and tick pet spray products containing benzisothiazolin-3-one registered in Canada all contain 0.0193% or less of benzisothiazolin-3-one. One concentrate product contains 0.096% benzisothiazolin-3-one. However, once it is diluted according to label directions (one part product to 19 parts water), the final product to be applied would contain only 0.0048% benzisothiazolin-3-one. Based on this, the PMRA requires no further mitigation measures with respect to residential exposure.

3.1.2.2 Exposure From Food and Drinking Water

Acute dietary risk is estimated by determining how much of a pesticide residue may be ingested with the daily diet and comparing this potential exposure to an acute reference dose, which is the dose at which an individual could be exposed over the course of one day and expect no adverse health effects. The acute reference dose is referred to as ARfD in Canada, and, in the RED, it is expressed as the acute population adjusted dose (aPAD). The ARfD or aPAD is based on a relevant endpoint from toxicology studies and on safety factors protective of the most sensitive subpopulation (see Appendix II).

Chronic dietary risk is estimated by determining how much of a pesticide residue may be ingested with the daily diet and comparing this potential exposure to an acceptable daily intake, which is the dose at which an individual could be exposed over the course of a lifetime and expect no adverse health effects. The acceptable daily intake is referred to as the ADI in Canada, and, in the RED, it is expressed as the chronic population adjusted dose (cPAD). The ADI is

based on a relevant endpoint from toxicology studies and on safety factors protective of the most sensitive subpopulation (see Appendix II).

In the United States, food could indirectly come into contact with benzisothiazolin-3-one as a result of its use as a preservative in paper coating and paper adhesives and as a slimicide in paper/pulp manufacturing. These uses are not registered in Canada and are not discussed here.

Dietary exposure could also result from the use of benzisothiazolin-3-one as a formulant in agricultural pesticide products. A quantitative drinking water assessment was not conducted since benzisothiazolin-3-one was not expected to be present in drinking water sources at substantial concentrations (i.e. breaks down readily in aerobic soils and only very small amounts may be applied to crops when it is used as a formulant in agricultural pesticide products).

For the formulant use, an unrefined, conservative assessment was conducted by the USEPA using the generic screening model for estimating inert ingredient (i.e. formulant) dietary exposure. It was assumed that 1,2-benzisothiazolin-3-one as a formulant was limited to a maximum concentration of 0.1% in any pesticide formulation and could not be applied at more than 0.02 kg per ha, that it was used on all commodities, that 100% of crops were treated and that residues would be present for every consumed commodity that was included in the Dietary Exposure Evaluation Model. Both low- and high-end exposures were found to represent less than 100% of the aPAD (5 to 84%) and cPAD (2 to 51%) for all population subgroups, with the exception of children 1 to 2 years old, who had an estimated exposure of 112% of the aPAD at the high end of exposure (22% at the low end of exposure). However, the USEPA did not consider dietary risk due to the formulant use to be of concern for any population subgroup based on the fact that the assessment was unrefined and extremely conservative in nature.

In Canada, benzisothiazolin-3-one generally occurs at a concentration of 0.1% or less when used as a formulant in other pesticide products. As a result, the RED adequately addressed potential exposure scenarios associated with the Canadian uses of benzisothiazolin-3-one (i.e. when used as a formulant in pesticides on agricultural crops). Thus, the conclusions derived from the RED are considered applicable to the Canadian situation. Based on this, the PMRA requires no further mitigation measures with respect to dietary exposure at this time.

3.1.2.3 Aggregate Risk Assessment

Aggregate risk combines the different routes of exposure to benzisothiazolin-3-one (i.e. from food and residential exposures).

The acute and chronic aggregate risk assessments combine the contributions from food exposure from use of both the active ingredient and formulant. For the formulant use, the USEPA selected the low range values based on the conservative nature of the risk assessment. Acute aggregate risk was acceptable at 17.1% of the aPAD for the general population and 44.1% of the aPAD for the most exposed subgroup, children aged 1 to 2 years. Chronic aggregate risk was acceptable at 12.2% of the cPAD for the general population and 31.8% of the cPAD for the most exposed subgroup, children aged 1 to 2 years.

Short- and intermediate-term aggregate risk assessments combined contributions from food and non-occupational exposure sources (dermal, inhalation, oral ingestion), including both the active ingredient and formulant use of benzisothiazolin-3-one. The aggregate risk index (ARI) method was used because different uncertainty factors had to be applied to the oral, dermal and inhalation endpoints. A risk index greater than or equal to one indicates a risk of no concern. Short-term ARIs for adults and children were 6.8 and 1.9, respectively, and intermediate-term ARIs for adults and children were 7.5 and 1.9, respectively, and were not of concern.

Overall, the Canadian aggregate exposure scenarios were adequately addressed by the USEPA aggregate risk assessment. Therefore, the USEPA aggregate exposure conclusions are considered applicable to the uses of benzisothiazolin-3-one in Canada.

3.1.3 Cumulative Effects

The USEPA has not determined whether benzisothiazolin-3-one has a common mechanism of toxicity with other substances or whether it shares a toxic metabolite produced by other substances. Therefore, it was assumed that benzisothiazolin-3-one does not share a common mechanism of toxicity with other substances, and a cumulative risk assessment was not required.

3.2 Environment

3.2.1 Environmental Risk Assessment

Laboratory studies showed that benzisothiazolin-3-one was stable to hydrolysis. However, based on a laboratory aerobic soil half-life of less than 24 hours in sandy loam, benzisothiazolin-3-one was not expected to be persistent in the environment. Benzisothiazolin-3-one was shown to exhibit moderate to strong binding to soil, with adsorption K_d values between 1.24 and 9.56, and was not expected to leach to groundwater. Bioaccumulation in aquatic organisms was also not expected based on the K_{ow} value.

The acute toxicity data for 1,2-benzisothiazolin-3-one ranged from low to moderately toxic to birds and mammals, moderately toxic to freshwater fish and invertebrates, and highly toxic to marine/estuarine invertebrates and green algae. The USEPA concluded that indoor uses of benzisothiazolin-3-one were not likely to result in unacceptable ecological risk to non-target organisms based on minimal exposure potential. The USEPA did not conduct any quantitative ecological risk assessments. Similarly, the use of 1,2-benzisothiazolin-3-one as a formulant occurs at no more than 0.1% of the formulation and is readily biodegraded in soil, greatly reducing the exposure potential for terrestrial and aquatic organisms. Runoff into surface water from the use of 1,2-benzisothiazolin-3-one as a formulant was also expected to be low. No mitigation measures were required.

3.2.2 Toxic Substances Management Policy Considerations

The management of toxic substances is guided by the 1995 federal Toxic Substances Management Policy, which puts forward a preventive and precautionary approach to deal with substances that enter the environment and could harm the environment or human health. The

policy provides decision makers with direction and sets out a science-based management framework to ensure that federal programs are consistent with its objectives. One of the key management objectives is virtual elimination from the environment of toxic substances that result predominantly from human activity and that are persistent and bioaccumulative. These substances are referred to in the policy as Track 1 substances.

The federal Toxic Substances Management Policy and PMRA Regulatory Directive DIR99-03, *The Pest Management Regulatory Agency's Strategy for Implementing the Toxic Substances Management Policy*, were taken into account during the re-evaluation of benzisothiazolin-3-one. The PMRA has reached the following conclusions:

- Benzisothiazolin-3-one is not bioaccumulative. The *n*-octanol–water partition coefficient (log K_{ow}) is 0.4, which is below the TSMP Track 1 cut-off criterion of ≥ 5.0. Benzisothiazolin-3-one was not found to be persistent. The aerobic soil half-life was less than 24 hours in sandy loam, which is below the TSMP Track 1 criterion of 180 days. Benzisothiazolin-3-one does not meet all Track 1 criteria; thus, it is not a candidate for Track 1 classification.

- Microcontaminant data were not submitted for all technical products. Data for Thor Acticide BIT Technical (Reg. No. 28122) is required.

  Two technical class products containing benzisothiazolin-3-one (Reg. No. 23197 and Reg. No. 25712) have been shown to contain low levels of polychlorinated dibenzo-dioxins (PCDDs). Low levels of polychlorinated dibenzofurans (PCDFs) were also detected in Reg. No. 23197. PCDDs and PCDFs substituted in at least the 2,3,7,8 positions have been identified in the Federal Government's Toxic Substances Management Policy as Track 1 substances. The PMRA is continuing its efforts to implement the Agency's strategy to manage Track 1 contaminants in pest control products (Regulatory Directive DIR99-03).

No other impurities of toxicological concern as identified in Regulatory Directive DIR98-04, Section 2.13.4, or TSMP Track 1 substances as identified in Regulatory Directive DIR99-03, Appendix II are expected to be present in the technical product of benzisothiazolin-3-one.

Formulant issues are being addressed through PMRA formulant initiatives and Regulatory Directive DIR2006-02, *Formulants Policy and Implementation Guidance Document,* published on 31 May 2006.

4.0 Proposed Re-evaluation Decision

The PMRA has determined that benzisothiazolin-3-one as an active ingredient in pest control products is acceptable for continued registration with the implementation of the proposed risk-reduction measures. These measures are required to further protect human health and the environment. The labels of Canadian end-use product must be amended to include the label statements listed in Appendix III. A submission to implement label revisions will be required within 90 days of finalization of the re-evaluation decision. No additional data are being requested at this time.

5.0 Supporting Documentation

PMRA documents, such as Regulatory Directive DIR2001-03, and DACO tables can be found on our website at www.pmra-arla.gc.ca. PMRA documents are also available through the Pest Management Information Service. Phone: 1-800-267-6315 within Canada or 1-613-736-3799 outside Canada (long distance charges apply); fax: 613-736-3798; e-mail: pmra_infoserv@hc-sc.gc.ca.

The federal TSMP is available through Environment Canada's website at www.ec.gc.ca/toxics.

The USEPA RED document for benzisothiazolin-3-one is available on the USEPA Pesticide Registration Status page at www.epa.gov/pesticides/reregistration/status.htm.

List of Abbreviations

ADI	acceptable daily intake
aPAD	acute population adjusted dose
ARfD	acute reference dose
ARI	aggregate risk index
bw	body weight
CAS	Chemical Abstracts Service
cPAD	chronic population adjusted dose
DACO	data code
g	gram(s)
ha	hectare(s)
IUPAC	International Union of Pure and Applied Chemistry
kg	kilogram(s)
K_d	adsorption coefficient
K_{ow}	*n*-octanol–water partition coefficient
L	litre(s)
m	metre(s)
m^3	metre(s) cubed
mg	milligram(s)
MOE	margin of exposure
NOAEL	no observed adverse effect level
Pa	Pascal(s)
PCDD	polychlorinated dibenzo-dioxin
p*K*a	-log10 acid dissociation constant
PMRA	Pest Management Regulatory Agency
PRVD	Proposed Re-evaluation Decision
RED	Reregistration Eligibility Decision
RfD	reference dose
TSMP	Toxic Substances Management Policy
USEPA	United States Environmental Protection Agency

Appendix I Registered Products Containing Benzisothiazolin-3-one as of 1 February 2008

Registration Number	Marketing Class	Registrant	Product Name	Formulation Type	Guarantee (%)
23197	Technical	Arch Chemicals, Inc.	Proxel Press Paste	Paste	72
24412	Technical (IMEP)	ISP Canada Inc.	Nuosept BIT	Wettable powder	82
25712	Technical	Clariant Corp.	Nipacide BIT Press Paste	Paste	75
28122	Technical	Thor GmbH	Thor Acticide BIT Technical	Solid	72
14683	Commercial	Arch Chemicals, Inc.	Proxel GXL Microbiostat Solution	Solution	19.3
25716	Commercial	Arch Chemicals, Inc.	Proxel DL Microbiostat Solution	Solution	9
27268	Commercial	Clariant Corp.	Nipacide BIT 20 Liquid	Solution	18.5
27301	Commercial	Clariant Corp.	Nipacide BIT 10 Liquid	Solution	9
27559	Commercial	Troy Chemical Corporation	Mergal K10N Liquid Industrial Biocide	Solution	9.5
27570	Commercial	Clariant Corp.	Nipacide BIT 20 DPG Liquid	Solution	18.5
28125	Commercial	Thor GmbH	Thor Acticide B20 Microbiocide Liquid	Solution	20
28126	Commercial	Thor GmbH	Thor Acticide BW20 Microbiocide Liquid	Solution	20
28158	Commercial	ISP Canada Inc.	Nuosept 495 Preservative	Solution	19
28196	Commercial	Dow Chemical Canada Inc.	Canguard BIT 20 DPG Preservative	Solution	18.5
28203	Commercial	Dow Chemical Canada Inc.	Bioban BIT 20 DPG Antimicrobial	Solution	18.5
28268	Commercial	Dow Chemical Canada Inc.	Canguard BIT 10 Preservative	Solution	9
28269	Commercial	Dow Chemical Canada Inc.	Bioban BIT 10 Antimicrobial	Solution	9
28413	Commercial	ISP Canada Inc.	Nuosept 497 Preservative	Solution	19
28823	Commercial	ISP Canada Inc.	Nuosept 498 Preservative	Solution	19

Appendix II Toxicological Endpoints for Benzisothiazolin-3-one Health Risk Assessments

Exposure Scenario	Dose (mg/kg bw/day)	Study	UF/SF or Target MOE[a]
Occupational short- and intermediate-term dermal	Oral NOAEL = 5 (41% dermal absorption)	Subchronic oral toxicity study in the dog	100
Occupational short- and intermediate-term inhalation	Oral NOAEL = 5 (100% absorption)	Subchronic oral toxicity study in the dog	100
Residential short- and intermediate-term dermal	Oral NOAEL = 5 (41% dermal absorption)	Subchronic oral toxicity study in the dog	100
Residential short- and intermediate-term inhalation	Oral NOAEL = 5 (100% absorption)	Subchronic oral toxicity study in the dog	100
Residential incidental oral	Oral NOAEL = 5	Subchronic oral toxicity study in the dog	300
Acute dietary	Oral NOAEL = 5	Subchronic oral toxicity study in the dog	300
	Chronic RfD = 0.017 mg/kg bw/day (i.e. acceptable daily intake)		
Chronic dietary	Oral NOAEL = 5	Subchronic oral toxicity study in the dog	300
	Chronic RfD = 0.017 mg/kg bw/day (i.e. acceptable daily intake)		

[a] UF/SF refers to total of uncertainty and/or safety factors for dietary assessments. MOE refers to desired margin of exposure for occupational or residential assessments.

Appendix III Label Amendments for Products Containing Benzisothiazolin-3-one

The label amendments presented below do not include all label requirements for individual end-use products, such as first aid statements, disposal statements, precautionary statements and supplementary protective equipment. Additional information on labels of currently registered products should not be removed unless it contradicts the above label statements.

The labels of end-use products in Canada must be amended to include the following statements to further protect workers and the environment.

I) The following statement must be included in the **PRECAUTIONS** section.

> Wear a long-sleeved shirt, long pants and chemical-resistant gloves when handling this product.

References

List of Studies/Information Submitted by Registrant

PMRA 1321382	1995, Technical Chemistry file - BZZ-CIO-1. Correspondence to Rex Toxopeus from R.L. Schauer Re NIPA Bit Press Paste Specifications, Analysis of 10 Consecutive Batches, UV-Visible Absorption Spectrum, DACO: 2.99, DACO 2.14
PMRA 1321394	Technical Chemistry file BZZ-CIO-1. Summary, Description of Beginning Materials, Discussion of the Formation of Impurities, Preliminary Analysis of Product Samples, Physical and Chemical Characteristics, Vapor Pressure, Octanol/Water Partition Coefficient, DACO 2.14, DACO 2.11
PMRA 1321378	2004, Technical Chemistry file - BZZ-CIO-1. Nipacide Bit Press Paste Transfer of Ownership, DACO: 2.13.3
PMRA 1494987	1,2-benzisothiazolin-3-one, Part 2 Specifications and Analytical Methodology, DACO: 2.1, 2.11, 2.12, 2.13, 2.14, 2.15, 2.16, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9
PMRA 1323912	Technical Chemistry file References 1 to 4. Physical/Chemical Characteristics of PROXEL Press Paste, Determination of Polychlorinated Dibenzo-p-diozins and Dibenzofurans, Biocides – Stability During Shelf Life and Proxel Press Paste: Nitrosamines., DACO: 2.13.4, 2.14
PMRA 1555543	1990, Proxel Press Paste: Chemical Characterisation of Material Representative of Huddersfield Works Manufacture - GLP Project 144, 144; RD010977C, DACO: 2.13.3
PMRA 1323914	Technical Chemistry file - References 1 to 4. Further information on the identity of impurities in PROXEL Press Paste, PROXEL Comparison of HPLC Impurity Profiles from Regulatory Studies 144, 306 and 267, Proxel Press Paste Process Change: Characterisation, DACO 2.13.3, 2.13.4
PMRA 768086	1999, Summary of Physical and Chemical Characteristics of Acticide BIT - Colour, Physical State, Odour, Melting Point, Boiling Point, Density or Specific Gravity, Water Solubility, Solvent Solubility, Vapour Pressure, Dissociation Constant, Octanol/Water, DACO 2.14
PMRA 768089	1999, Melting Point Determination of Acticide BIT, 702731, MRID: N/S, DACO: 2.14.4
PMRA 768092	1999, Water Solubility of Acticide BIT, 705431, MRID: N/S, DACO: 2.14.7

PMRA 768094 1999, Vapor Pressure of Acticide BIT, 702696, MRID: N/S, DACO: 2.14.9

PMRA 768095 2001, Acticide BIT Dissociation Constant, SSL00801, MRID: N/S, DACO: 2.14.10

PMRA 768096 1999, Octanol / Water Partition Coefficient of Acticide BIT, 702718, MRID: N/S, DACO: 2.14.11

PMRA 768098 1999, Stability of Acticide BIT (Stability Temperature and Metals), 706026, MRID: N/S, DACO: 2.14.13,2.14.14